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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,350	09/05/2003	Robert C. Ladner	D2033-701910	8718

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EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
12/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@ll-a.com
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Office Action Summary	Application No.	Applicant(s)	
	10/656,350	LADNER ET AL.	
	Examiner	Art Unit	
	JEFFREY S. LUNDGREN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 22 September 2009.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18,20-28 and 39-44 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18,20-28 and 39-44 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/22/09.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A Request for Continued Examination under 37 CFR § 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR § 1.114, and the fee set forth in 37 CFR § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR § 1.114. Applicant's submission filed on September 22, 2009, has been entered.

Previous Grounds of Rejection – Withdrawn

The previous grounds of rejection raised in the Office Action mailed on September 22, 2009, have been withdrawn in view of Applicants' Declaration and amendments filed in the RCE received on September 22, 2009.

Claim Rejections - 35 USC § 103 – New in View of Amendment

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

<u>Claims 1-9, 13, 15-17, 20-27 and 39-44, are obvious over Ladner, Anderson</u>:

Claims 1-9, 13, 15-17, 20-27 and 39-44, under 35 U.S.C. § 103(a) as being unpatentable over Ladner *et al.*, U.S. Patent No. 5,403,484 A, issued on April 4, 1995, in view of Anderson, U.S. Patent No. 6,649,419 B1, issued on November 18, 2003, and Chandrashekar *et al.*, U.S. Patent No. 5,854,051, issued on December 29, 1998.

The claimed invention is generally directed towards affinity filter screening of phage from a library using a target immobilized to solid substrate. The phage from the library that have affinity towards the immobilized target bind to the solid substrate through the target, while the unbound phage are removed/washed away. The target-bound phage are then used in the bound form to infect host cells, replicated, and screening is repeated using the same target-immobilized substrate, as amended.

More specifically, claim 1 is directed to a method of selecting phage that encode a target binding protein from a plurality of display phage, the method comprising:

a) forming a mixture comprising a plurality of diverse display phage, a target, and a support, wherein each phage of the plurality displays a heterologous protein component on its surface and each phage includes a nucleic acid encoding the heterologous protein component, the heterologous protein component being a member of a set of diverse protein components;

b) forming phage immobilized to the support, each of which comprises a phage from the plurality which binds the target and the target immobilized to the support;

c) separating phage that do not bind to the target from the phage immobilized to the support via binding to the target;

d) contacting host cells with the phage immobilized to the support so that the host cells are infected by the phage immobilized to the support to yield a first population of infected cells;

e) producing replicate phage from the infected cells in the presence of the target immobilized to the support, thereby forming replicate phage immobilized to the support via binding to the target of step (a);

f) separating replicate phage that do not bind to the target of step (a) from the replicate phage immobilized to the support; and

g) contacting host cells with the replicate phage immobilized to the support so that host cells are infected with the replicate phage immobilized to the support to yield a second population of infected cells.

As in part (a) of claim 1, Ladner teaches a method for screening a library of diverse phage (*i.e.*, KLMUT – a diverse library of over 1 x 10^5 phage – col. 143, lines 57-60), each phage displaying heterologous protease inhibitors which are considered diverse protein components, such as EpiNE1 through EpiNE8 (col. 142, line 14 through col. 143, line 56) having binding affinity for a target (*i.e.*, human neutrophil elastase) immobilized to a solid substrate (*i.e.*, agarose beads) – see col. 144, lines 15-36. As in part (b) of claim 1, this section of Ladner teaches that the phage bind to the support through the target; as in part (c), phage that do not bind the target are eluted away (*i.e.*, separated); as in part (d), the particle-bound phage are infected into XL1-Blue™ cells (col. 144, lines 28-30); as in step (e), the previous infection reaction produced 348 plaques which were pooled for further affinity selection with the immobilized HNE-beads, and as in step (f) the non-binding phage are separated from the phage bound to the HNE-beads, and as in step (g), the host cells are contacted with these beads and infected with the phage to form a second population of cells.

As in claims 2 and 3, Ladner teaches recovering the second population of infected cells and recovering the phage from those cells (col. 144, lines 37-41).

Claim 4 is directed towards a third replication by repeating steps (e) through (g); Ladner teaches the third replicated series of steps (col. 144, lines 41-60).

As in claim 8, Ladner teaches adding an additional amount of target (*i.e.*, adding to an additional amount of a 50% slurry of beads - col. 144, lines 34-36).

As in claim 9, Ladner teaches use of the MB phage which is an M13 type phage (col. 118, lines 5-33) – Landner teaches that these phage typically produce between 100 and 1000 progeny (col. 55, lines 40-44), and therefore meet the limitations of the claim.

As in claim 13, Ladner teaches a diverse library of 10^5 phage with 97.4% of the approximately 97.4% possible DNA constructs – col. 143, lines 57-61.

As in claim 15, the phage of the KLMUT library each have a gene that allows for replication in the host cell (see col. 55, lines 28-44; col. 118, lines 5-35; and col. 144, lines 18-36).

As in claim 16, Ladner teaches that the phage may be selected from a phagemid (col. 76, lines 39-40), and that the use of a helper phage can be carried out (col. 60, lines 44-46).

As in claim 17, Ladner teaches the use of competing ligands to enhance identifying phage with desired properties (col. 98, lines 43-49)

As in independent claim 20, Ladner teaches (a) providing a bacteriophage library that comprises a plurality of bacteriophage members - (*i.e.*, KLMUT – a diverse library of over 1 x 10^5 phage – col. 143, lines 57-60;

(b) selecting a subset of the bacteriophage members – the step of binding the library of phage to the beads taught in Ladner; each phage displaying heterologous protease inhibitors which are considered diverse protein components, such as EpiNE1 through EpiNE8 (col. 142, line 14 through col. 143, line 56) having binding affinity for a target (*i.e.*, human neutrophil elastase) immobilized to a solid substrate (*i.e.*, agarose beads) – see col. 144, lines 15-36;

(c) infecting host cells with the members of the subset – Ladner teaches that the particle-bound phage are infected into XL1-Blue™ cells (col. 144, lines 28-30);

(d) amplifying members of the subset under at least one of the following conditions: (1) fewer than 5000 progeny phage are produced for each phage member selected in step (b) – Ladner teaches use of the MB phage which is an M13 type phage (col. 118, lines 5-33) – Ladner teaches that these phage typically produce between 100 and 1000 progeny (col. 55, lines 40-44);

(e) selecting a subset of amplified members, thereby identifying the desired members of the bacteriophage library – Ladner teaches the affinity maturation process wherein the selected phage reintroduced to cells and propagate, which are further selected and propagated (*i.e.*, amplified), and identification of clones having the greatest affinity (col. 144, lines 37-61).

As in claim 21, the amplification process and selection process of Ladner occur in the presence of the target as the bead-bound phage infect the host cells and progeny are produced, wherein the progengy phage bind the target (col. 144, lines 37-61). As in claims 22 and 23, Ladner teaches that the target (which can be the cells binding to the solid support as defined by Applicants' specification – see specification page 0038) binds to the solid support during amplification; contacting the library to the target and solid support, wherein the bacteriophage library members bind to the target through the solid support (*i.e.*, beads) – see col. 144, lines 18-36.

As in independent claim 24, Ladner teaches a method for selecting a nucleic acid that encodes a binding protein comprising:

(a) providing a library of phage that each have a heterologous protein component that is diverse among the phage of the plurality, physically attached to the phage, and accessible – Ladner teaches a method for screening a library of diverse phage (*i.e.*, KLMUT – a diverse library of over 1 x 10^5 phage – col. 143, lines 57-60), each phage displaying heterologous protease inhibitors which are considered diverse protein components, such as EpiNE1 through EpiNE8 (col. 142, line 14 through col. 143, line 56) having binding affinity for a target (*i.e.*, human neutrophil elastase) immobilized to a solid substrate (*i.e.*, agarose beads) – see col. 144, lines 15-36;

(b) contacting phage of the library to a target – as noted above, Ladner teaches that the library of phage are introduced to the bead-immobilized target HNE;

(c) performing one or more cycles of:

i) forming phage immobilized to a support, each of which comprises (1) a phage that binds to the target by its heterologous protein component and (2) the target immobilized to a support – Ladner teaches that certain optimized heterologous proteins, such as EpiNE7.8 (col. 144, lines 50-61), bind to the immobilized HNE target,

ii) separating phage that do not bind to the target from the phage immobilized to the support via binding to the target – Ladner teaches that the phage that do not bind to the target are washed away, leaving behind phage that bind the target,

iii) contacting phage from the phage immobilized to the support with host cells so that the host cells are infected by the phage from the immobilized to the support – Ladner teaches that these phage that are bound to the target on the beads are used to infect the XL1-Blue™ cells (col. 144, lines 28-47), and

iv) producing phage from the infected cells in the presence of target, the produced phage being replicates of phage that bind to the target – Ladner teaches that the recovered phage are replicates of the initial phage, but comprise a smaller library greater affinity/selectivity towards the HNE target, such as EpiNE7.8 as noted above; and

(d) recovering the nucleic acid encoding the heterologous protein of one or more produced phage - Ladner teaches recovering the nucleic acid (col. 144, lines 47-61).

As in claim 25, the conditions of separating the phage vary in stringency – Ladner teaches varying the pH (col. 144, lines 26-28).

As in claims 26 and 27, Ladner repeats the cycles of affinity maturation at least three times (col. 144, lines 15-61).

Although Ladner teaches performing his isolation of select phage bound to ligand-modified beads in reactions vessels, Ladner does not explicitly teach the use of the same target as carried out in step (a), such as a reusable target immobilized to a bead, nor the reduced phage plating time of 4 hours. Ladner also does not explicitly teach that the reactions are carried out in the same vessel, such as the steps of (a) through (g), or the steps of (d) to (e) in claims 5 and 6, respectively; and although Ladner discloses the addition of further target immobilized to the bead (*i.e.*, HNE), Ladner does not explicitly suggest that the reaction can be performed without additional target, as in claim 7.

Anderson teaches a method for using magnetic beads to isolate biological components of interest, wherein the component of interest binds to a target that is attached to the bead. Anderson teaches that the reactions used with the beads can be used to recover the target, and further utilize the target component of interest by manipulating the bead that it is attached to, and does not require further addition of more target-immobilized beads:

> "Once the protein is adsorbed to the beads, directly or via an affinity ligand, the composition is one of a denatured protein bound to the bead. The beads can be further manipulated by use of appropriate magnetic fields to perform processes such as digestion with protease, exposure to antibody mixtures in order to select those antibodies that specifically bind to the protein, and exposure to other proteins that may or may not be found to bind to the original protein."

Anderson, col. 11, lines 29-37; and the beads can be reacted and maintained in a single reaction vessel:

> "Instead of moving the beads to other vessels, one may collect the beads and aspirate, wash and change the solution in the same vessel for performing the next step."

Anderson, col. 29, lines 8-10.

Chandrashekar is directed towards parasitic helminth asparaginase proteins; parasitic helminth asparaginase nucleic acid molecules, including those that encode such asparaginase proteins; antibodies raised against such asparaginase proteins; and compounds that inhibit parasitic helminth asparaginase activity. The present invention also includes methods to obtain such proteins, nucleic acid molecules, antibodies, and inhibitory compounds. Also included in the present invention are therapeutic compositions comprising such proteins, nucleic acid molecules, antibodies and/or inhibitory compounds as well as the use of such therapeutic compositions to protect animals from diseases caused by parasitic helminths. One experimental approach for expressing the desired proteins from the library of nucleic acids involves a 4 hour incubation of the phage (see Example 4, paragraph bridging cols. 28 and 29, <u>especially col. 29 lines 1-4</u>).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Ladner and Anderson are directed towards techniques that utilize beads/reaction supports for the isolation of biological components that have affinity for given ligands. One of ordinary skill in the art would have recognized the advantages of the single vessel approach used by Anderson in the phage targeting, isolation and growth as taught by Ladner, namely, the ease of use of having the selected biological component of interest contained to a single location that easily permits rapid addition and removal of reagents and reaction byproducts. Furthermore, one of ordinary skill in the art would have recognized the reusable nature of the beads as taught by Anderson, and recognized these advantages in the method of Ladner, such as reduced quantities of reagents. Regarding the time limitations such as the “4 hours” or less time as in claims 39-44, such adjustments are merely routine experimental parameters as demonstrated by Chandrashekar with predictable outcomes (*e.g.*, lower numbers of colonies). Therefore the invention as a whole was *prima facie* obvious at the time it was invented.

<u>*Claims 1-10, 12-17, 20-28 and 39-44 are obvious over Ladner, Anderson, Chandrashekar and Janda*</u>:

Claims 1-10, 12-17, 20-28 and 39-44, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ladner *et al.*, U.S. Patent No. 5,403,484 A, issued on April 4, 1995, in view of Anderson, U.S. Patent No. 6,649,419 B1, issued on November 18, 2003; Chandrashekar *et al.*, U.S. Patent No. 5,854,051, issued on December 29, 1998; and Janda, U.S. Patent No. 5,571,681 A, issued on November 5, 1996.

The limitations of claims 1-9, 13, 15-17, 20-27 and 39-44, and the corresponding teachings in Ladner and Anderson are presented above, and are hereby incorporated into the instant rejection.

Although Ladner provides certain general guidelines and conditions for reaction times involving the phage, Ladner does not explicitly teach reaction times of leas than 4 hours for step (e) or steps (d) and (f), as in claims 10 and 12, or the cycles being less than 8 hours as in claim 28; nor does Anderson. Ladner also does not explicitly teach a change in the temperature upon the producing step as in claim 14; nor does Anderson.

Janda generally teaches the use of covalent conjugates that are immobilized by attachment to a substrate through a solid phase and are easily separated from unconjugated elements of the combinatorial library by stringent washing. Janda generally teaches combinatorial libraries employing phagemid-display are particularly preferred since such phagemids include genetic material for identifying and amplifying conjugated catalysts. In describing the reactions for contact phage with the host cell, incubating the cell, and expressing the phage in the host cell, the processes can be carried out in less than four hours, such as the 15 minutes to infect the XL1-Blue™ cells, and the 2 hour culturing – note that the overnight cell selection with kanamycin is not required due to the beads being able to select the phage of interest an only captures progeny phage produced from the first round of binding to the bead that produced in the host cell (col. 25, lines 37-50). As in claim 14, Janda teaches going from room temperature during infection to 37 degrees C during incubation (col. 25, lines 37-50).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Ladner, Anderson and Janda are directed towards the use of methods for affinity selection of phage to a library of targets using bead-based strategies. Although Ladner does not explicitly recite the claimed time limitations or temperature change, such adjustments to those parameters are considered routine in the art, as

exemplified by Janda, and are well within the purview of the ordinary artisan, especially considering that there is nothing in Applicants' disclosure that would present any objective indicia of non-obviousness (*e.g.*, there are no teachings of unexpected results based on the claimed limitations). Therefore, the invention as whole was *prima facie* obvious at the time it was invented.

Claims 1-9, 13, 15-18, 20-27 and 39-44, are obvious over Ladner, Anderson, Chandrashekar and McCafferty:

Claims 1-9, 13, 15-18, 20-27 and 39-44, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ladner *et al.*, U.S. Patent No. 5,403,484 A, issued on April 4, 1995, in view of Anderson, U.S. Patent No. 6,649,419 B1, issued on November 18, 2003; McCafferty *et al.*, U.S. Patent No. 5,969,108 A, issued on October 19, 1999, and Chandrashekar *et al.*, U.S. Patent No. 5,854,051, issued on December 29, 1998.

The limitations of claims 1-9, 13, 15-17, 20-27 and 39-44, and the corresponding teachings in Ladner, Anderson and Chandrashekar are presented above, and are hereby incorporated into the instant rejection.

Although Ladner teaches the use of phage for producing a library of heterologous proteins with improved affinity, Ladner does not teach the use of mutator host strains as claimed in claim 18.

McCafferty teaches a member of a specific binding pair (sbp) is identified by expressing DNA encoding a genetically diverse population of such sbp members in recombinant host cells in which the sbp members are displayed in functional form at the surface of a secreted recombinant genetic display package (rgdp) containing DNA encoding the sbp member or a polypeptide component thereof, by virtue of the sbp member or a polypeptide component thereof being expressed as a fusion with a capsid component of the rgdp. The displayed sbps may be selected by affinity with a complementary sbp member, and the DNA recovered from selected rgdps for expression of the selected sbp members (see Abstract). McCafferty also uses subsequent rounds of selection and mutagenesis (col. 6, lines 1-5). Regarding mutagenesis,

McCafferty teaches the value that mutator strains provide for combinatorial chemistry when using phage:

> "It will often be necessary to increase the diversity of a population of genes cloned for the display of their proteins on phage or to mutate an individual nucleotide sequence. Although in vitro or in vivo mutagenesis techniques could be used for either purpose, a particularly suitable method would be to use mutator strains. A mutator strain is a strain which contains a genetic defect which causes DNA replicated within it to be mutated with respect to its parent DNA. Hence if a population of genes as gene III fusions is introduced into these strains it will be further diversified and can then be transferred to a non-mutator strain, if desired, for display and selection."

McCafferty, col. 9, lines 50-61.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Ladner, Anderson, Chandrashekar and McCafferty are directed towards developing mutant heterologous polypeptides with phage display, wherein the selected phage have improved affinity/activity towards a given target. One of ordinary skill in the art would have been motivated to utilize a mutator strain as taught by McCafferty for the host cells of Ladner during the affinity maturation process because the mutator strains provide a convenient way to increase the diversity of genes used by the phage to display the library member. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Claims 1-17, 20-28 and 39-44 are obvious over Ladner, Anderson, Chandrashekar Janda and Steinbuchel:

Claims 1-17, 20-28 and 39-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladner, Anderson, Chandrashekar and Janda as applied to claims 1-4, 8-10, 12-17, 20, 21 and 23-28 above, and further in view of Steinbuchel *et al.*, U.S. Patent No. 6,022,729, issued on February 8, 2000.

The limitations of claims 1-10, 12-17, 20-28 and 39-44, and the corresponding teachings of Ladner, Anderson and Janda are detailed in the rejection above, and are hereby incorporated into the instant rejection.

Although each of Ladner and Janda each teach the use of the host cells XL1-Blue™ cells for preparing a phage library, and Janda teaches certain reaction times and temperatures, neither teaches that the host cells divide less than seven times as in claim 11.

Steinbuchel is directed to the use of certain host cells, such as XL1-Blue™ cells, for producing mutant polypeptide strains, wherein the host cells have been transfected with various constructs, such as pSKC07 and pSK2665 (see col. 14, lines 27-55). Over the course of cell growth, Steinbuchel shows the growth rate of the XL1-Blue™ cells under standard conditions (see Figure 5). As can be seen from Figure 5, the time for the host cell population to double, or equivalently carry out one division on average, is between about 30 minutes (closed symbols) and less than four hours (open symbols)[1].

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Ladner and Janda are directed towards the use of methods for affinity selection of phage to a library of targets using bead-based strategies, and Steinbuchel is directed towards the use of the same host cells for producing mutant polypeptides. Although Ladner does not explicitly recited the claimed time limitations or temperature change (nor Anderson), such adjustments to those parameters are considered routine in the art, as exemplified by Janda, or the growth rate of XL1-Blue ™ cells within the time frame of Janda resulting in less than seven divisions, and are well within the purview of the ordinary artisan, especially considering that there is nothing in Applicants' disclosure that would present and objective indicia of non-obviousness (*e.g.*, there are no teachings of unexpected results based on the claimed limitations). Therefore, the invention as whole was *prima facie* obvious at the time it was invented.

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[1] The graph is plotted as optical density which equivalent to an absorbance measurement produced from the XL1-Blue™ cells, where A = abc; (A, absorbance; a, molar absorptivity; b, path length, and c, concentration of host cells)

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusions

No claim is allowable.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

– therefore, a doubling in the OD is a result of a doubling of the concentration/number of the host cells, or one cell division.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey S. Lundgren/
Primary Examiner, Art Unit 1639